COULD PLATELET INDICES HAVE PREDICTIVE VALUE IN HENOCH-SCHÖNLEIN PURPURA?

TROMBOSİT İNDEKSLERİ HENOCH-SCHÖNLEİN PURPURASINDA PREDİKTİF DEĞERE SAHİP OLABİLİR Mİ?

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Öz

Amaç: Biz trombosit indekslerinin Henoch-Schönlein purpurasında klinik seyir ve tutulum tipi bakımından prediktif değere sahip olup olmadığını araştırmayı amaçladık. Gereç ve Yöntem: Henoch-Schönlein purpuralı hastaların verileri geriye dönük olarak incelendi. Hastalar tutulum tiplerine göre sınıflandırıldı. Tanı anında ve klinik iyileşme sonrası trombosit indeksleri kaydedildi. Tutulum tipine göre ayrılmış her bir grubun ve kontrol grubunun verileri incelendi. Bulgular: Henoch-Schönlein purpuralı hastalarda trombosit sayısı ve trombosit dağılım genişliği değerleri kontrol grubuyla karşılaştırıldığında önemli derecede artmıştı. Bununla birlikte ortalama trombosit hacmi değerleri önemli derecede düşüktü. Tutulum tipleri arasında trombosit indeksleri bakımından farklılık yok iken, aynı indeksler bazal değerlerle karşılaştırıldığında klinik iyileşme sonrası önemli derecede değişmekteydi. Tartışma: Trombosit indeksleri Henoch-Schönlein purpurasının klinik seyirinden belirgin şekilde etkilenir. Trombosit indeksleri Henoch-Schönlein purpurasının teşhisinde ve klinik seyirinin takibinde faydalı bir belirteç olabilir.

Anahtar Kelimeler

Gastrointestinal Tutulum; Henoch-Schönlein Purpurası; Ortalama Trombosit Hacmi; Trombosit Dağılım Genişliği; Renal Tutulum

Abstract

Aim: We aimed at investigating whether platelet indices have predictive value for clinical course and type of involvements in Henoch-Schönlein purpura. Material and Method: Data from patients with Henoch-Schönlein purpura were retrospectively investigated. Patients were classified according to types of involvements. Platelet indices were recorded at the time of diagnosis and after clinical remission. Data from each group according to types of involvements and healthy controls were investigated. Results: Platelet counts and platelet distribution width values were significantly increased in patients with Henoch-Schönlein purpura compared to controls, whereas mean platelet volume values were significantly lower. While no difference existed among types of involvements concerning platelet indices, the same indices were significantly altered after clinical remission, compared to baseline. Discussion: Platelet indices are considerably affected in the course of Henoch-Schönlein purpura. Platelet indices could be beneficial as a surrogate marker in the diagnosis and clinical course of Henoch-Schönlein purpura.

Keywords

Gastrointestinal Involvement; Henoch-Schönlein Purpura; Mean Platelet Volume; Platelet Distribution Width; Renal Involvement

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Introduction

Henoch-Schönlein purpura (HSP) is one of the most common types of systemic vasculitis in childhood [1]. Palpable purpura is the mandatory diagnostic criteria for HSP and also accompanied by various symptoms and findings such as diffuse abdominal pain, any biopsy showing predominant IgA deposition, arthritis or arthralgia, hematuria and proteinuria [2]. Although HSP is often a self-limited condition, renal involvement is fairly common in pediatric patients [3]. However, renal involvement infrequently may become chronic and lead to permanent organ damage [4,5]. Gastrointestinal (GI) bleeding is one of the major complications which may cause serious morbidity, and occurs in 18-52% of the patients.

In HSP, thrombocytosis is associated with disease severity, particularly with GI bleeding [6]. Commonly used as a measure of platelet (PLT) size, mean platelet volume (MPV) indicates the rate of PLT production and PLT activation [7]. Previously, MPV values have been studied in patients with hypertension, rheumatoid arthritis, familial Mediterranean fever, diabetes mellitus, obesity, during acute coronary syndrome, acute rheumatic fever and HSP with GI bleeding [6,8,9].

To the best of our knowledge, PLT counts, MPV and platelet distribution width (PDW) values have yet to be assessed all in one study in patients with HSP. In the present study, we also aimed at investigating whether PLT counts, MPV and PDW values in HSP patients are of a predictive value for Henoch-Schönlein nephritis and GI involvements, as well as comparing those in HSP patients with healthy controls.

Material and Method

Data of all children hospitalized with the diagnosis of HSP during the acute stage in the unit of pediatric nephrology between January 2012 and May 2015 were reviewed. Patients with a chronical hematologic, collagenous tissue or myeloproliferative disorders and those with the use of such medications as oral anticoagulant, aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs) were excluded out of the study.

The following data were collected using a computerized patient database: complete blood count including white blood cell (WBC), PLT counts, MPV and PDW values; erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) values at the time of diagnosis and after clinical remission.

All patients were classified according to the EULAR/PRES diagnostic criteria for HSP, and diagnoses and treatment regimes administered were recorded [2]. GI involvement was defined as abdominal pain plus occult blood in stool or the existence of melena or hematochezia. Renal involvement was defined as the presence of hematuria and/or proteinuria. While patients with skin and/or joint, mild GI and renal involvements were treated with NSAIDs, those with severe GI and renal involvements were treated with oral prednisolone. The control group was composed of 50 healthy children. Complete blood count parameters of healthy children were obtained from the same computerized database. The study was approved by the local ethics committee of our institution.

Statistical analysis was performed using the Statistical Package for Social Sciences for Windows (SPSS, Chicago, IL), and results were expressed as mean±SD. Normal distributed data were assessed by the Kolmogorov-Smirnov test. The analysis was based on non-parametric statistical methods due to the small size of samples and abnormal distribution of variables. On the other hand, the data determined to be normally distributed after the Kolmogorov-Smirnov test was evaluated via parametric statistical methods. The Mann-Whitney U or Student's t tests for paired comparisons were used for subgroup analysis when appropriate. $p<0.05$ was accepted to be statistically significant.

Results

One hundred and seventy children, 120 patients and 50 healthy controls, were included into the study. The general clinical characteristics of patient and control groups were shown in Table 1. No statistically significant difference was found between the groups as to age and sex ($p>0.05$); however, the boys/girls ratio was 1.5 in patient group ($p<0.05$).

One hundred and twenty patients had all palpable purpura, and skin and/or joint involvements were identified in 61 patients, GI involvement in 30, renal involvemet in 21, and both GI and renal involvements in 8. WBC, PLT counts and PDW values were significantly increased in patients with HSP when compared to

Table 1. Clinical and laboratory characteristics of patient and control groups, and frequency of involvement in patient group

	Patients (n=120) Mean±SD or n (%)	Controls (n=50) Mean±SD or n (%)	p
Age, years	7.7±3.4	7.7±4.2	>0.05
Sex			
Boys	72 (60)	27 (54)	>0.05
Girls	48 (40)	23 (46)	>0.05
Involvement			
Skin and/or joint	61 (50.8)	-	
GI	30 (25)	-	
Renal	21 (17.5)	-	
GI and Renal	8 (6.7)	-	
Parameters			
WBC (count x103/mm3)	11.7±4.7	9.3±3.1	<0.05
PLT (count x 103/mm3)	393.4±136.1	311.6±79.2	<0.05
MPV (fL)	8.56±1.40	9.73±0.87	<0.05
PDW	25.11±15.56	10.97±1.48	<0.05
CRP (mg/L)	24.3±30.6	6.9±6.8	<0.05
ESR (mm/hour)	31.9±22.9	14.2±9.9	<0.05

GI, gastrointestinal; WBC, white blood cell; PLT, platelet; MPV, mean platelet volume; PDW, platelet distribution width; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate

Table 2. Comparison of laboratory findings at baseline and after remission in patient group

Parameters	Baseline (Mean±SD)	After remission (Mean±SD)	p
WBC (count x 103/mm3)	11.7±4.7	10.2±4.4	<0.05
PLT (count x 103/mm3)	393.4±136.1	359.3±102.7	<0.05
MPV (fL)	8.56±1.40	8.85±1.45	>0.05
PDW	25.11±15.56	17.72±11.68	<0.05
CRP (mg/L)	24.3±30.6	13.2±19.1	<0.05
ESR (mm/hour)	31.9±22.9	22.7±19.4	<0.05

WBC, white blood cell; PLT, platelet; MPV, mean platelet volume; PDW, platelet distribution width; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate

Table 3. Laboratory findings of involvement types in patient group

Parameters	Skin and/or joint n=61 Mean±SD	GI n=30 Mean±SD	Renal n=21 Mean±SD	GI and Renal n=8 Mean±SD
WBC (count x 103/mm3)	11.08±3.64	12.73±4.94	11.83±6.91	12.91±4.76
PLT (count x 103/mm3)	375.6±138.1	443.8±151.1	370.4±90.6	400.5±134.33
MPV (fL)	8.71±1.43	8.3±1.27	8.69±1.20	8.1±2.06
PDW	23.39±15.31	30.68±14.97	23.02±16.92	22.8±13.44
CRP (mg/L)	25.3±33.0	20.9±26.3	20.8±26.7	38.4±37.3
ESR (mm/hour)	33.4±22.7	27.3±15.7	37.3±33.6	24.8±9.4

WBC, white blood cell; PLT, platelet; MPV, mean platelet volume; PDW, platelet distribution width; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate

controls ($p<0.05$), whereas MPV values were significantly lower ($p<0.05$).

WBC, PLT counts and PDW values were significantly decreased in patients with HSP after clinical remission when compared to baseline ($p<0.05$). In contrast, an increase was detected in MPV, although statistically insignificant ($p>0.05$) (Table 2).

While mean PLT counts, MPV and PDW values were found to be significantly different when all involvement types were compared one by one with those in control group ($p<0.05$), no difference was observed among mean WBC, PLT counts, MPV and PDW values, and acute phase reactants in patient group as to the types of involvements ($p>0.05$) (Table 3).

Sixty-five percent of patients were treated with prednisolone, and 35% with NSAIDs. While all patients with skin and/or joint involvement were given NSAIDs, 46.7% of patients with GI involvement were treated with NSAIDs, 53.3% with prednisolone. Whereas 14.3% of patients with renal involvement were treated with NSAIDs, 85.7% were administered prednisolone. Additionally, patients with both GI and renal involvements were treated with prednisolone, except for one. In seven patients (25%) with renal involvement, either nephritic or nephrotic involvement was seen to develop in the long-term. Of these seven patients, five were with renal involvement, and two with both GI and renal involvements.

Discussion

HSP is one of the most common types of systemic vasculitis in childhood with a slightly higher incidence in boys than in girls [10]. In patients presenting with HSP, renal involvement is encountered at the rate of some 20-40% [3,10]. About 20% of patients with Henoch-Schönlein nephritis, accounting for 7% of all HSP cases, develop either a nephritic or nephrotic syndrome [1]. In our study, while the boys/girls ratio was 1.5 in patient group, the rates of renal, and both GI and renal involvements were 17.5 and 6.7%, respectively. Although the rate of developing a nephritic or nephrotic syndrome was 5.8%, the same rate was 25% among patients with renal involvement. While Makay et al. reported the rates of abdominal pain and GI bleeding as 53.5% and 30.2% respectively, the same rates were reported as 57.9 for abdominal pain and 17.6% for GI bleeding by Chang et al [6,11]. However, GI and renal involvements were found to be 25 and 6.7% in our study, respectively.

PLT counts, MPV and PDW values have yet to be evaluated all in one study in children with HSP previously, and to the best of our knowledge, our study is the first to investigate these values all in one study. In our study, while WBC, PLT counts and PDW values were increased in children with HSP, compared to healthy control subjects, MPV values were found to be lower. However, WBC, PLT counts and PDW values were significantly decreased in patient group after remission, whereas MPV values were inversely increased, although not statistically significant. Based on these findings, we considered that WBC, PLT counts, and MPV and PDW values could be beneficial as diagnostic and clinical follow-up criteria in HSP, and that the alterations, especially in PDW values were more remarkable, compared to those in MPV values.

Overproduction of pro-inflammatory cytokines and acute-phase reactants is known to suppress the size of platelets by interfering with megakaryopoiesis with subsequent release of small size platelets from the bone marrow [6,8]. Bleeding diathesis is more frequently witnessed in individuals with low platelet size due to lower functional capabilities of small platelets [6]. Therefore, it may be speculated that the increases in PLT counts and PDW values with subsequent decrease in MPV values all derive from the devastation in PLT function probably due to vascular endothelial disfunction and cytokine storm. The clinical reflection of this condition is seen as purpura, GI bleeding and hematuria. The fact that PLT indices begin returning close-to-normal values after remission, namely, during the chronical phase when the inflammation subsides supports the above speculation. We also hypothesized that impaired vessel integrity could lead to PLT damage during vasculitis, and that the treatment with salicylates and/or steroids may play a role in the amelioration of thrombocyte values by supressing the vascular inflammation. However, these physiopathological considerations were well beyond the scope of this study.

As consistent with our findings, Makay et al. reported that WBC and PLT counts were higher, and MPV values were lower in HSP patients, compared to healthy controls [6]. Thrombocytosis, in the same study, was also shown to be associated with more severe disease in HSP, particularly with gastrointestinal hemorrhage. In our study, PLT counts and PDW values, although statistically insignificant, were higher in patients with GI involvement, compared to those with other types of involvements, but MPV values were lower. We found no statistically significant difference among PLT indices as to the types of involvements. As one of our limitations, this condition could have arised from limited number of participants in our study. Within all types of involvements, however, mean PLT counts, and MPV and PDW values were significantly different from those in healthy controls.

Current treatment options are mainly based on anecdotal evidence. Therefore, if treatment options are to be improved, better predictive prognostic markers and better understanding of pathophysiology are required. In this preliminary study, we have shown that PLT indices are considerably affected in the course of HSP. We consider that PLT indices may be utilized in the diagnosis of HSP and in the trace of its activation as a surrogate marker. Still, comprehensive studies also including histopathology are needed in order to enlighten the role that such changes in PLT indices play in the physiopathology of HSP.

Competing interests

The authors declare that they have no competing interests.

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